Microcephaly, seizures, and developmental delay

Microcephaly, seizures, and developmental delay (MCSZ) is a condition characterized by an abnormally small head size (microcephaly) and neurological problems related to impaired brain development before birth. Affected individuals typically have recurrent seizures (epilepsy) beginning in infancy and delayed development of motor skills, such as sitting and walking. Speech is also delayed, and some affected individuals are never able to speak. Intellectual disability and behavior problems, primarily hyperactivity, are also common features of MCSZ. Rarely, individuals with MCSZ also have poor balance and coordination (ataxia).

Frequency

MCSZ is a rare disorder. Its prevalence is unknown.

Causes

MCSZ is caused by mutations in the *PNKP* gene. This gene provides instructions for making an enzyme that is critical for repairing broken DNA strands. DNA breaks may be caused by potentially harmful molecules (such as reactive oxygen species) produced during normal cellular functions, natural and medical radiation, or other environmental exposures. They may also occur when chromosomes exchange genetic material in preparation for cell division. At the site of damage, the PNKP enzyme modifies the broken ends of the DNA strands so that they can be joined back together.

PNKP gene mutations lead to production of an unstable enzyme that is quickly broken down in the cell. Shortage of the PNKP enzyme prevents efficient repair of damaged DNA. Nerve cells seem especially susceptible to such damage. It is thought that DNA damage that accumulates during development before birth leads to the death of nerve cell precursors, impairing normal brain growth and causing microcephaly and the other neurological features of MCSZ.

Accumulated DNA damage in nerve cells in the brain after birth, particularly the part that coordinates movement (the cerebellum), likely underlies ataxia. It is unclear why some people have cerebellar nerve degeneration after birth in addition to impaired brain development before birth and others do not. Researchers suspect that additional genetic factors play a role.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- EIEE10
- epileptic encephalopathy, early infantile, 10
- MCSZ

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Early infantile epileptic encephalopathy 10
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3150667/

Other Diagnosis and Management Resources

- MedlinePlus Encyclopedia: Head Circumference
  https://medlineplus.gov/ency/article/002379.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Epilepsy - Children
  https://medlineplus.gov/ency/article/007681.htm
- Encyclopedia: Head Circumference
  https://medlineplus.gov/ency/article/002379.htm
- Encyclopedia: Microcephaly
  https://medlineplus.gov/ency/article/003272.htm
- Encyclopedia: Microcephaly (image)
  https://medlineplus.gov/ency/imagepages/17256.htm
- Health Topic: Brain Malformations
  https://medlineplus.gov/brainmalformations.html

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Ataxias and Cerebellar or Spinocerebellar Degeneration
  https://www.ninds.nih.gov/Disorders/All-Disorders/Ataxias-and-Cerebellar-or-Spinocerebellar-Degeneration-Information-Page
- National Institute of Neurological Disorders and Stroke: Epilepsy
  https://www.ninds.nih.gov/Disorders/All-Disorders/Epilepsy-Information-Page
- National Institute of Neurological Disorders and Stroke: Microcephaly
  https://www.ninds.nih.gov/Disorders/All-Disorders/Microcephaly-Information-Page

Educational Resources

- Boston Children's Hospital: Microcephaly
  http://www.childrenshospital.org/conditions-and-treatments/conditions/m/microcephaly
- Centers for Disease Control and Prevention: Facts About Developmental Disabilities
  https://www.cdc.gov/ncbddd/developmentaldisabilities/facts.html
- Centers for Disease Control and Prevention: Facts About Intellectual Disability
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- KidsHealth from Nemours: Seizures
  https://kidshealth.org/en/parents/seizure.html
- Lucille Packard Children's Hospital at Stanford: Microcephaly
  https://www.stanfordchildrens.org/en/topic/default?id=microcephaly-90-P02610
- MalaCards: microcephaly, seizures, and developmental delay
  https://www.malacards.org/card/microcephaly_seizures_and_developmental_delay
- World Health Organization: Epilepsy
  https://www.who.int/en/news-room/fact-sheets/detail/epilepsy

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD)
  https://www.aaidd.org/
- Ataxia UK
  https://www.ataxia.org.uk/
- CURE Epilepsy
  https://www.cureepilepsy.org/
- Medical Home Portal: Seizures/Epilepsy
  https://www.medicalhomeportal.org/diagnoses-and-conditions/seizures-epilepsy
- National Ataxia Foundation
  https://ataxia.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28MCSZ%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- MICROCEPHALY, SEIZURES, AND DEVELOPMENTAL DELAY
  http://omim.org/entry/613402

Medical Genetics Database from MedGen

- Early infantile epileptic encephalopathy 10
  https://www.ncbi.nlm.nih.gov/medgen/462017

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Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/microcephaly-seizures-and-developmental-delay

Reviewed: June 2018
Published: June 23, 2020

Lister Hill National Center for Biomedical Communications
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National Institutes of Health
Department of Health & Human Services